

REMARKS

Claims 1-8 are pending in the present application and were rejected. Claims 1, 3 and 6 are herein amended. Claim 2 is herein cancelled without prejudice.

Applicants' Response to Claim Rejections under 35 U.S.C. §112

Claims 1-8 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is the position of the Office Action that the terms “functional unit,” “a reporter unit,” and “biofunctional unit” are not defined by the specification. In response to the previously filed remarks, the Office Action states that paragraph [0040] of the specification “does not set limits on said terms; it merely sets forth examples.” The Office Action goes on to state that “a particular embodiment appearing in the written description may not be read into a claim when the claim language is broader than the embodiment.”

In response, Applicants herein amend claims 1 and 6 in order to clarify the claimed subject matter. This is because in paragraph [0040] “functional group” is defined as including a color-fluorescing unit, a reporter unit or a biofunctional molecule. Applicants herein amend claims 1 and 6 accordingly.

As to the merits of the rejection, Applicants respectfully submit that the proposed amended claims are sufficiently definite. As explained by MPEP 2173.02, “Definiteness of claim language must be analyzed, not in a vacuum, but in light of:

- (A) The content of the particular application disclosure;
- (B) The teachings of the prior art; and
- (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.”

As such, Applicants respectfully submit that the claim language is sufficiently definite to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement. Contrary to the Office Action’s statement, the claimed embodiment is not broader than the disclosure. The possible R groups are defined, without limitation, by their function. Such functional groups are well known to those having ordinary skill in the art. The “color-fluorescing unit” of claim 1 or 6 includes as “R” any group which, upon release, fluoresces color. The “reporter unit” of claim 1 or 6 includes as “R” any group which, upon release, acts as a reporter of an antigen or antibody. The “biofunctional molecule” of claim 1 or 6 includes any group which, upon release, regulates biological functions *in vivo*. A pharmaceutical preparation and an antibody are examples of such a “biofunctional molecule.” Accordingly, Applicants respectfully submit that amended claims 1 and 6 fully comply with the requirements of 35 U.S.C. §112.

Finally, Applicants note that the rejection states that “it is unclear whether the limitations within the parenthesis are part of the claimed invention.” However, the parentheses were deleted from the claims in the Amendment filed on July 3, 2008. Thus, this aspect of the rejection should be withdrawn.

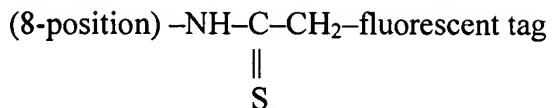
Applicants' Response to Claim Rejections under 35 U.S.C. §103

Claims 1-5 were rejected under 35 U.S.C. §103(a) as being unpatentable over Urdea et al. (U.S. Patent No. 4,910,300) in view of Sorbi et al. (U.S. Patent No. 4,797,480).

It is the position of the Office Action that Urdea discloses the embodiments as claimed, with the exception of teaching purine nucleotides. The Office Action relies on Sorbi to provide this teaching.

Urdea is directed at a method for making nucleic acid probes. Urdea states that due to the fact that nucleotide modification is “a difficult and sensitive procedure,” nucleotide substitution positions are typically limited “to the 5-position of a pyrimidine and the 8-position of a purine.” See column 2, lines 13-24. However, Urdea is directed at a nucleotide modification in which a nucleotide is modified at the 4-position of a pyrimidine and, optionally, modified at the 5-position. See column 2, lines 42-49. The modification includes the substitution of $\text{NH}-(\text{CH}_2)_x\text{R}^2\text{-R}^1$ for the NH_2 at the 4-position of a pyrimidine. See Figure 1. Urdea teaches that R^1 is a reactive group, while R^2 is “an amide, thioether or disulfide linkage or combination thereof.” See column 3, lines 18-25. Urdea does not disclose any specific examples of purine substitutions.

Sorbi is directed at biologically active fluorescent cyclic nucleotides. As shown by formula (VII) at column 2, lines 43-58, Sorbi teaches a purine having a substitution at the 8-position. The substitution (L) is a fluorescent group bound through a thioacetamido linkage. See column 2, lines 60-62. The substitution (L) is represented by the following:



Thus, the (L) group of Sorbi is different from the moiety of the claimed embodiments, which is represented by (8-position)-NH-(CH₂)₂-NH-R. Therefore, Sorbi merely teaches that fluorescent tags can be attached to the 8-position of purines. Accordingly, Sorbi does not provide any substantial additional teachings beyond Urdea's disclosure that nucleotide substitutions are typically limited to the 8-position of purines.

In response, Applicants first respectfully submit that the combination of Urdea and Sorbi does not disclose or suggest the embodiment as claimed. Claim 1 is herein amended in order to incorporate the subject matter of claim 2. Thus, claim 1 requires that the moiety of the claimed embodiments is represented by (8-position)-NH-(CH₂)₂-NH-R. However, neither Urdea nor Sorbi teach this moiety. In Urdea, the moiety may be one in which the alkyl group ((CH₂)_x) and the reactive group (R¹) are linked by an *amide* group. However, in the claimed embodiment, the alkyl group ((CH₂)₂) and the color-fluorescing unit, reporter unit or biofunctional molecule (R) are linked by an *amine* group. Thus, Urdea does not disclose the moiety as claimed, regardless of its position on a nucleotide. Additionally, as is clear from the discussion above, the moiety of Sorbi (substitution (L)) is significantly different from the claimed moiety. Therefore, Applicants respectfully submit that the combination of references does not disclose or suggest the embodiments as claimed.

Furthermore, Applicants respectfully submit that it would not have been obvious to modify the combination of Urdea and Sorbi in order to arrive at the embodiment as claimed.

Both Urdea and Sorbi are directed at a moiety in which a label (which corresponds to the R group as claimed) *is stably retained at the base of the nucleotide*. On the other hand, the claimed embodiments are directed at a moiety in which a R group linked to the 8-position of guanine via the linker —NH—(CH₂)₂—NH— *is released by oxidization*. One having ordinary skill in the art would have had no reason to modify a moiety for *retaining* a label in order to arrive at a moiety for *releasing* a label.

Finally, Applicants respectfully submit that even if, *arguendo*, Urdea taught the —NH—(CH₂)₂—NH—R moiety as claimed with the exception of the 8-position location on a guanine, it would not have been obvious to modify such a teaching in order to arrive at the claimed embodiments. As specifically noted by Urdea:

It is widely recognized that nucleotide modification is a difficult and sensitive procedure, as any modification reaction has to be mild enough to leave the RNA or DNA molecules intact, while giving a modified nucleotide product which can participate in normal base pairing and stacking interactions. These considerations typically limit nucleotide substitution positions to the 5-position of a pyrimidine and the 8-position of a purine. Column 2, lines 15-23. (emphasis added).

As recently explained by the Supreme Court, “when there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp.” *KSR Int'l v. Teleflex Inc.*, 82 USPQ2d 1385, 1397 (2007) (emphasis added). However, as explained by Urdea, the art of nucleotide modification is unpredictable. As such, it cannot be said that a person of ordinary skill in the art has good reason to modify guanine using the nucleotide substitution of Urdea, which is applied to pyrimidines. One having ordinary skill in

the art would be unable to predict whether a moiety which, when substituted at the 5-position of a pyrimidine, maintains the normal functions of a nucleotide, would maintain the normal function of the nucleotide when substituted at the 8-position of a purine. Similarly, one having ordinary skill in the art would not be able to predict whether a moiety which, when substituted at the 4-position of a pyrimidine, maintains the normal functions of a nucleotide, would maintain the normal function of the nucleotide when substituted at the 5-position of a pyrimidine, and whether a moiety which, when substituted at the 4-position of a pyrimidine, maintains the normal functions of a nucleotide, would maintain the normal function of the nucleotide when substituted at the 8-position of a purine. In other words, it cannot be said that nucleotide substitutions are “interchangeable.” Therefore, for at least the above reasons, Applicants respectfully submit that the combination of the cited art does not disclose or suggest the embodiments as claimed. Favorable reconsideration is respectfully requested.

Claims 6-8 were rejected under 35 U.S.C. §103(a) as being unpatentable over Urdea in view of Sorbi, and further in view of Okamoto et al. (Angew. Chem. Int. Ed. (2003), Vol. 42, pages 2502-2504).

It is the position of the Office Action that the combination of Urdea and Sorbi discloses the embodiments as claimed, with the exception of teaching releasing the R group moiety by oxidation. The Office Action relies on Okamoto to provide this teaching.

In response, Applicants respectfully submit that claim 6 is patentable for at least similar reasons as discussed above with respect to claim 1. Applicants respectfully reiterate that since the

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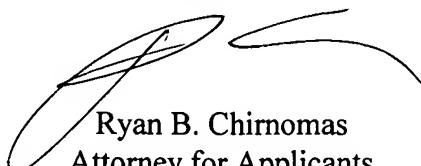
nucleic acids of Sorbi and Urdea can bind to their targets without dissociating or releasing their label, there is no reason why one having ordinary skill in the art would have looked to the teachings of Okamoto, since the teachings of Okamoto would be unnecessary in the context of Sorbi and Urdea. Therefore, for at least the above reasons, Applicants respectfully submit that the combination of the cited art does not disclose or suggest the embodiments as claimed. Favorable reconsideration is respectfully requested.

For at least the foregoing reasons, the claimed invention distinguishes over the cited art and defines patentable subject matter. Favorable reconsideration is earnestly solicited.

Should the Examiner deem that any further action by applicants would be desirable to place the application in condition for allowance, the Examiner is encouraged to telephone applicants' undersigned attorney.

If this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. The fees for such an extension or any other fees that may be due with respect to this paper may be charged to Deposit Account No. 50-2866.

Respectfully submitted,
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